

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
27 May 2004 (27.05.2004)

PCT

(10) International Publication Number
WO 2004/044001 A3

(51) International Patent Classification⁷: **C07K 14/47**,
C12N 5/10, A61K 38/17, G01N 33/50, C07K 16/18,
C12N 15/11

(21) International Application Number:
PCT/IB2003/005718

(22) International Filing Date:
11 November 2003 (11.11.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
0226251.7 11 November 2002 (11.11.2002) GB

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(81) Designated States (*national*): AE, AG, AL, AM, AT, AU,
AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU,
CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE,
GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR,
KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK,
MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT,
RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR,
TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (*regional*): ARIPO patent (BW, GH,
GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW),
Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),
European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE,
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE,
SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA,
GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declaration under Rule 4.17:

— *of inventorship (Rule 4.17(iv)) for US only*

Published:

— *with international search report*
— *before the expiration of the time limit for amending the
claims and to be republished in the event of receipt of
amendments*

(88) Date of publication of the international search report:
29 July 2004

*For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.*

(54) Title: ACETYLATED HMGB1 PROTEIN

(57) Abstract: An isolated multiply acetylated protein HMGB1; or a variant or fragment thereof, or a polynucleotide encoding therefor.



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INTERNATIONAL SEARCH REPORT

PCT/IB 03/05718

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07K14/47 C12N5/10 A61K38/17 G01N33/50 C07K16/18
C12N15/11

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

BIOSIS, EPO-Internal, EMBASE, WPI Data, SEQUENCE SEARCH, MEDLINE, EMBL

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	STERNER R ET AL: "STUDIES OF ACETYLATION AND DEACETYLATION IN HIGH MOBILITY GROUP PROTEINS IDENTIFICATION OF THE SITES OF ACETYLATION IN HIGH MOBILITY GROUP PROTEIN 1" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 254, no. 22, 1979, pages 11577-11583, XP002279281 ISSN: 0021-9258 the whole document --- -/--	1-55

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *Z* document member of the same patent family

Date of the actual completion of the international search

12 May 2004

Date of mailing of the international search report

17/06/2004

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INTERNATIONAL SEARCH REPORT

PCT/IB 03/05718

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>DATABASE EMBL 'Online! "HMGB1 protein and mRNA" retrieved from EBI Database accession no. NP_002119 XP002279285 the whole document -& DATABASE EMBL 'Online! retrieved from EBI Database accession no. NM_002128 XP002282370 the whole document</p>	1-55
Y	<p>POLEVODA B ET AL: "The diversity of acetylated proteins" GENOME BIOLOGY 2002 UNITED KINGDOM, vol. 3, no. 5, 2002, pages 0006.1-0006.6, XP002279282 ISSN: 1465-6906 the whole document</p>	1-55
Y	<p>GARDELLA STEFANIA ET AL: "The nuclear protein HMGB1 is secreted by monocytes via a non-classical, vesicle-mediated secretory pathway." EMBO REPORTS, vol. 3, no. 10, October 2002 (2002-10), pages 995-1001, XP002279283 ISSN: 1469-221X (ISSN print) the whole document</p>	1-55
Y	<p>SCAFFIDI PAOLA ET AL: "Release of chromatin protein HMGB1 by necrotic cells triggers inflammation" NATURE, MACMILLAN JOURNALS LTD. LONDON, GB, vol. 418, no. 6894, 11 July 2002 (2002-07-11), pages 191-195, XP002261326 ISSN: 0028-0836 the whole document</p>	1-55
Y	<p>THOMAS J O ET AL: "HMG1 and 2, and related 'architectural' DNA-binding proteins" TIBS TRENDS IN BIOCHEMICAL SCIENCES, ELSEVIER PUBLICATION, CAMBRIDGE, EN, vol. 26, no. 3, 1 March 2001 (2001-03-01), pages 167-174, XP004229458 ISSN: 0968-0004 the whole document</p>	1-55
X	<p>WO 99/59609 A (VANDER WAY LIMITED ;BARTORELLI ALBERTO (IT)) ,25 November 1999 (1999-11-25) claim 7</p>	44

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INTERNATIONAL SEARCH REPORT

PCT/IB 03/05718

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 00/47104 A (PICOWER INST MED RES) 17 August 2000 (2000-08-17) abstract ---	33-40, 44 .
P, X	BONALDI TIZIANA ET AL: "Monocytic cells hyperacetylate chromatin protein HMGB1 to redirect it towards secretion." EMBO (EUROPEAN MOLECULAR BIOLOGY ORGANIZATION) JOURNAL, vol. 22, no. 20, 15 October 2003 (2003-10-15), pages 5551-5560, XP002279284 ISSN: 0261-4189 (ISSN print) the whole document ---	1-55
P, X	WO 03/026691 A (BIANCHI MARCO ;MANFREDI ANGELO (IT); SAN RAFFAELE CENTRO FOND (IT)) 3 April 2003 (2003-04-03) the whole document -----	1-55

INTERNATIONAL SEARCH REPORT

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Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 33-37, 41, 43-45, 47-55 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☒ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Present claims 12-19, 23-37, and 42-55 relate to a compounds defined by reference to a desirable characteristic or property, namely modulation of acetylated HMGB1.

The claims cover all compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compound by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the antibodies and antisense molecules.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

PCT/IB 03/05718

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
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